

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization  
International Bureau



(43) International Publication Date  
22 August 2002 (22.08.2002)

PCT

(10) International Publication Number  
**WO 02/064562 A1**

(51) International Patent Classification<sup>7</sup>: **C07D 207/34, A01N 43/36**

(21) International Application Number: **PCT/EP02/01344**

(22) International Filing Date: 8 February 2002 (08.02.2002)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:  
0103258.0 9 February 2001 (09.02.2001) GB

(71) Applicant (for all designated States except US): **SYNGENTA PARTICIPATIONS AG [CH/CH]**; Schwarzwaldallee 215, CH-4058 Basel (CH).

(72) Inventor; and

(75) Inventor/Applicant (for US only): **WALTER, Harald [CH/CH]**; Syngenta Crop Protection AG, Schwarzwaldallee 215, CH-4058 Basel (CH).

(74) Agent: **BASTIAN, Werner**; Syngenta Participations AG, Intellectual Property, P.O.Box, CH-4002 Basel (CH).

(81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.

(84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

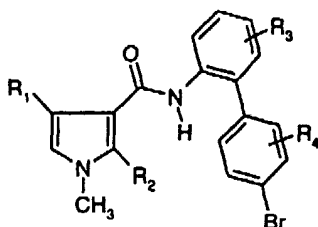
**Published:**

- with international search report
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

WO 02/064562 A1

(54) Title: **PYRROLECARBOXAMIDES FOR THE USE AS FUNGICIDES**



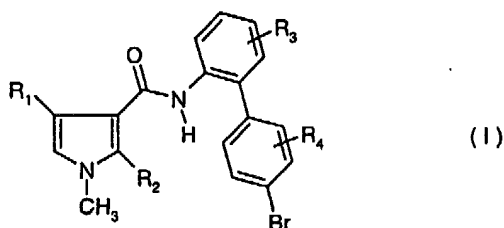
(1)

(57) Abstract: The invention concerns novel pyrrolocarboxamide of formula (I) wherein R<sub>1</sub> is CF<sub>3</sub>, CF<sub>2</sub>H or CFH<sub>2</sub>, R<sub>2</sub> is hydrogen or fluoro; R<sub>3</sub> is hydrogen or fluoro; and R<sub>4</sub> is hydrogen, fluoro, chloro, bromo, methyl, CF<sub>3</sub>, OCF<sub>3</sub> or SCF<sub>3</sub>. The compounds of formula (I) have plant-protective properties and are suitable for protecting plants against infestations by phytopathogenic microorganisms.

## PYRROLECARBOXAMIDES FOR THE USE AS FUNGICIDES

The present invention relates to novel pyrrolicarboxamides which have microbiocidal activity, in particular fungicidal activity. The invention also relates to the preparation of these substances, to agrochemical compositions which comprise at least one of the novel compounds as active ingredient, to the preparation of the compositions mentioned and to the use of the active ingredients or compositions in agriculture and horticulture for controlling or preventing infestation of plants by phytopathogenic microorganisms, preferably fungi.

The pyrrolicarboxamides of the present invention have the general formula I



wherein

R<sub>1</sub> is CF<sub>3</sub>, CF<sub>2</sub>H or CFH<sub>2</sub>;

R<sub>2</sub> is hydrogen or fluoro;

R<sub>3</sub> is hydrogen or fluoro; and

R<sub>4</sub> is hydrogen, fluoro, chloro, bromo, methyl, CF<sub>3</sub>, OCF<sub>3</sub> or SCF<sub>3</sub>.

Surprisingly, it has now been found that the compounds of formula I exhibit improved biological properties which render them more suitable for the practical use in agriculture and horticulture.

Where asymmetrical carbon atoms are present in the compounds of formula I, these compounds are in optically active form. The invention relates to the pure isomers, such as enantiomers and diastereomers, as well as to all possible mixtures of isomers, e.g. mixtures of diastereomers, racemates or mixture of racemates.

Preferred embodiments of compounds of formula I are those wherein

- 2 -

$R_1$  is  $CF_3$ ,  $CF_2H$  or  $CFH_2$ ; or

$R_1$  is  $CF_3$ ; or

$R_2$  is hydrogen or fluoro; or

$R_2$  is hydrogen; or

$R_2$  is fluoro; or

$R_3$  is hydrogen or fluoro; or

$R_3$  is hydrogen; or

$R_3$  is fluoro; or

$R_4$  is hydrogen, chloro, methyl,  $CF_3$  or  $OCF_3$ ; or

$R_4$  is hydrogen or methyl; or

$R_4$  is hydrogen, or

$R_2$ ,  $R_3$  and  $R_4$  are all hydrogen.

Within the group of compounds of formula I those compounds are preferred wherein

$R_1$  is  $CF_3$ ,  $CF_2H$  or  $CFH_2$ ;

$R_2$  is hydrogen or fluoro;

$R_3$  is hydrogen or fluoro; and

$R_4$  is hydrogen, chloro, methyl,  $CF_3$  or  $OCF_3$  (subgroup A).

Within the subgroup A are those compounds preferred wherein

$R_1$  is  $CF_3$ ,  $CF_2H$  or  $CFH_2$ ;

$R_2$  is hydrogen;

$R_3$  is hydrogen or fluoro; and

$R_4$  is hydrogen, chloro, methyl,  $CF_3$  or  $OCF_3$  (subgroup A1).

Another group of compounds of formula I within the subgroup A are those wherein

$R_1$  is  $CF_3$ ,  $CF_2H$  or  $CFH_2$ ;

$R_2$  is fluoro;

$R_3$  is hydrogen or fluoro; and

$R_4$  is hydrogen, chloro, methyl,  $CF_3$  or  $OCF_3$  (subgroup A2).

Among these subgroups, those compounds are preferred wherein  $R_2$ ,  $R_3$  and  $R_4$  are all hydrogen.

Preferred individual compounds are:

1-methyl-4-trifluoromethyl-1H-pyrrole-3-carboxylic acid (4'-bromobiphenyl-2-yl) amide;

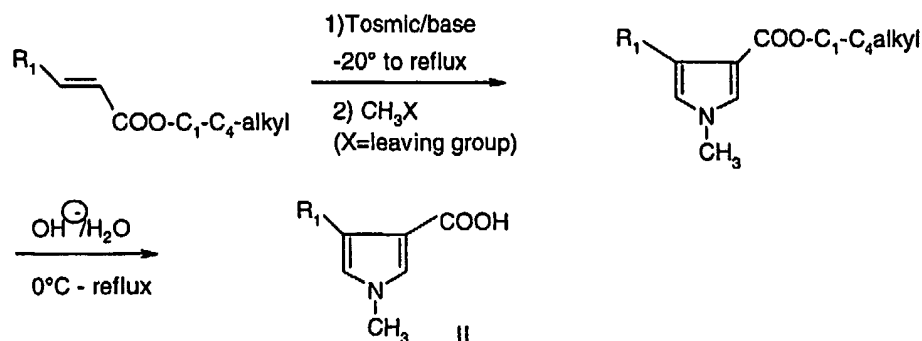
1-methyl-4-difluoromethyl-1H-pyrrole-3-carboxylic acid (4'-bromobiphenyl-2-yl) amide.

The compounds according to formula I may be prepared according to the following reaction in schemes. (Ac designates an acetyl group).

A) Synthesis of the pyrrole carboxylic acids :

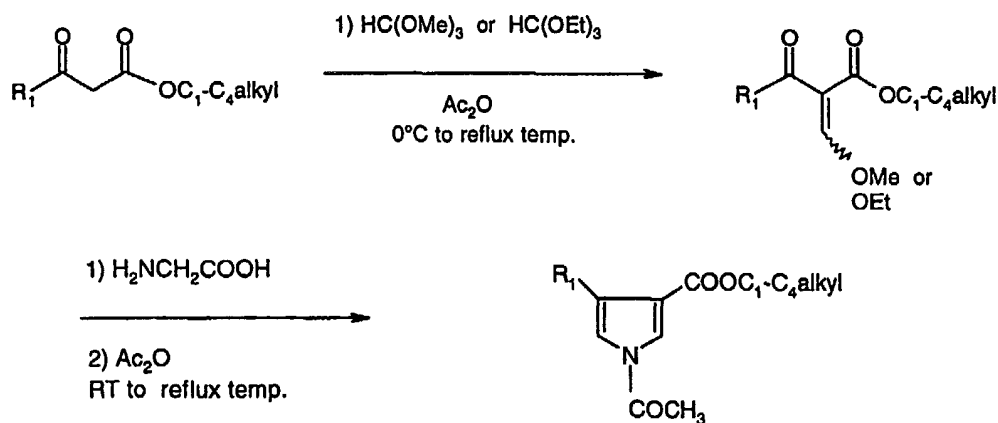
Route 1 (Tosmic-route)

Scheme 1

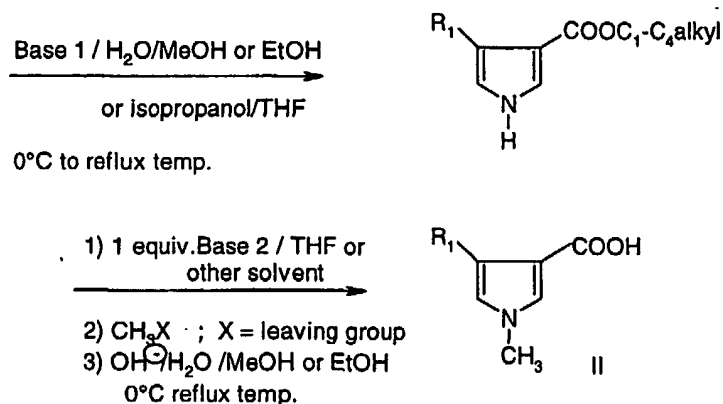


Route 2 (Trifluoroacetoacetic acid-route, analogous to JP-07157466)

Scheme 2



- 4 -



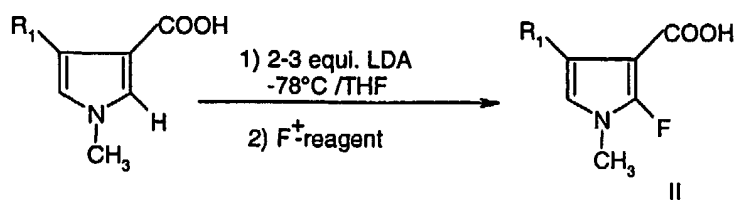
Base 1 =  $\text{NaHCO}_3$ ,  $\text{Na}_2\text{CO}_3$ ,  $\text{KHCO}_3$ ,  $\text{K}_2\text{CO}_3$ ,  $\text{CaCO}_3$  and other bases

Base 2 =  $\text{NaOH}$ ,  $\text{KOH}$ ,  $\text{NaH}$ ,  $\text{KH}$ ,  $n\text{-BuLi}$  and others

The synthesis of the pyrrole carboxylic acids of formula II wherein  $\text{R}_2 = \text{H}$  is described in WO-00/09482.

The synthesis of the pyrrole carboxylic acids of formula II wherein  $\text{R}_2$  is fluoro may be conducted according to the Schemes 2A or 2B.

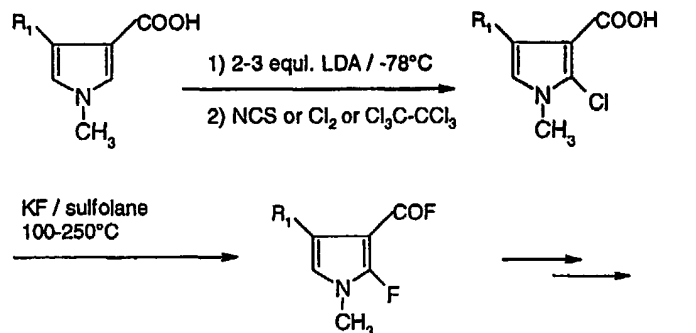
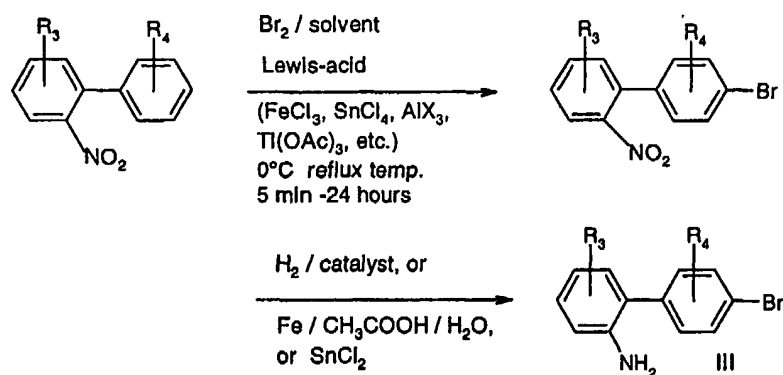
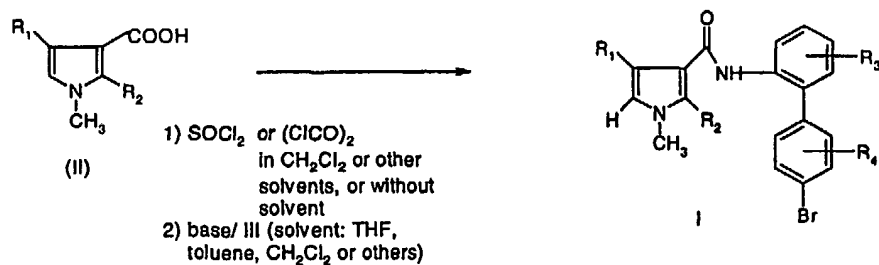
#### Scheme 2A



$\text{F}^+$ -reagents = N-fluoro-bis(phenylsulfonyl)amine, N-fluoro-N-methyl-toluene-4-sulfonamide,  
 2-fluoro-3,3-dimethyl-2,3-dihydro-1,2-benzisothiazole-1,1-dioxide,  
 1-fluoro-sym.-collidiniumtetrafluoroborate

LDA = lithiumdiisopropylamide

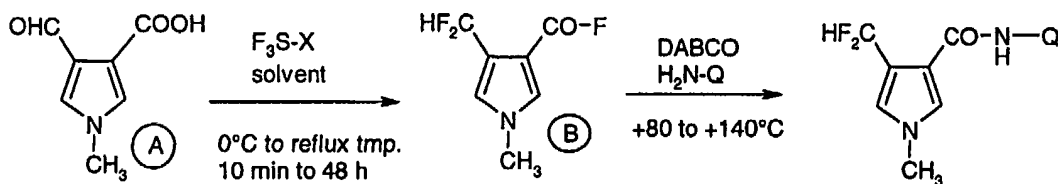
- 5 -

**Scheme 2B****B) synthesis of the amine III****Scheme 3**(AlX<sub>3</sub> is preferably AlCl<sub>3</sub>; solvent: water, DMF, THF,  $\text{CH}_2\text{Cl}_2$ ,  $\text{CHCl}_3$ ,  $\text{ClCH}_2\text{CH}_2\text{Cl}$ , etc.)**C) Synthesis of the amides****Scheme 4**Base =  $\text{N}(\text{C}_2\text{H}_5)_3$ , Hünig-base,  $\text{Na}_2\text{CO}_3$ ,  $\text{K}_2\text{CO}_3$  and others

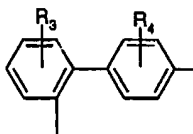
The pyrrole carboxylic acid II reacts with an activating agent such as thionyl chloride, phosphorous pentachloride or oxalic acid (or oxalyl) chloride in the presence of a solvent at a temperature between 0°C and reflux temperature and a reaction time of 30 minutes to 24 hours to give the corresponding acid chloride. Representative solvents are toluene, benzene, xylene, hexane, cyclohexane chloroform or methylenechloride. The obtained acyl chloride are normally not isolated. The new carboxamides of formula I are preferably obtained by reacting the activated pyrrolecarboxylic acid with an aromatic amine of formula III in the presence of a solvent like toluene, benzene, xylene, hexane, cyclohexane chloroform or methylenechloride and in the presence of an acid binding agent like triethylamine, Hünig base, sodium carbonate, potassium carbonate or sodium hydrogen carbonate at a temperature between 0°C and reflux temperature. Preferably the entire reaction sequence of scheme 4 is conducted as a single-vessel reaction.

The carboxylic acid fluoride intermediates of formula II wherein R<sub>1</sub> is CHF<sub>2</sub> may be obtained according to the following reaction route:

**Scheme 5:**



wherein Q is radical



as defined as part of formula I and X is F,

-N(CH<sub>3</sub>)<sub>2</sub>, -N(C<sub>2</sub>H<sub>5</sub>)<sub>2</sub>, -N(CH<sub>2</sub>CH<sub>2</sub>OCH<sub>3</sub>)<sub>2</sub> or . The reagents F<sub>3</sub>S-X are known,

e.g. from J.Org.Chem, 1999, (64), 7048.

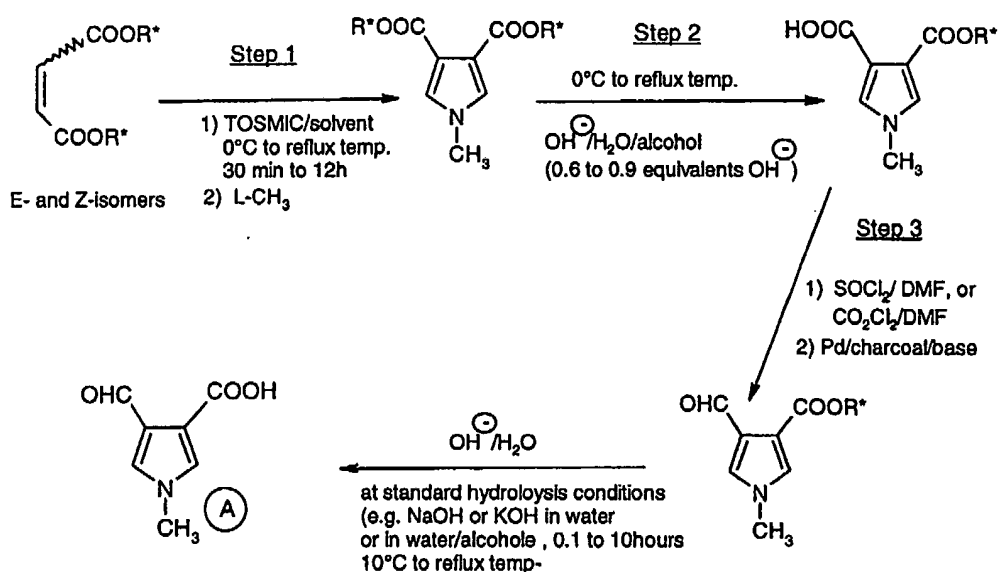
The last reaction step of Scheme 5 comprises a coupling (amidation) reaction which is advantageously conducted in the presence of 1 to 2 equivalents of a sterically hindered base like DABCO (1,4-diazabicyclo[2.2.2]octane) in a few drops of acetonitrile as a contact medium, by heating the reaction mixture for 2 to 3 hours to a temperature of 80°C to 140°C

- 7 -

until the reaction has taken place. After colling routine work-up procedure yields the final product of formula I wherein  $R_1$  is  $\text{CHF}_2$ .

The compound B and the synthesis thereof has especially been created for the production of the active ingredients of the present invention, and therefore represent further features of this invention. Likewise the novel compound A and the preceding esters are part of this invention. Compound A may be obtained as follows.

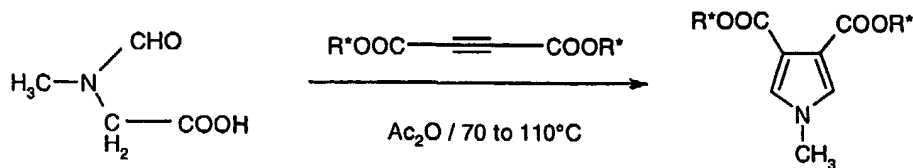
Scheme 6:



wherein  $R^*$  is  $\text{C}_1\text{-C}_6\text{alkyl}$ , or  $\text{Si}(\text{C}_1\text{-C}_6\text{alkyl})_3$ , and L is a leaving group like a halogen atom, -O-Tos, etc.. Reaction Step 3 is a modified version of a Rosenmund reaction, which is not yet known in the art, and thus represents another feature of this invention. Specifics are reactant combinations  $\text{SOCl}_2/\text{DMF}$  or oxalic acid dichloride/DMF, DMF in catalytic amount, optional inert solvent, in the first step and in the second step: reducing conditions like Pd on carbon at a temperature between 0°C and +10°C, preferably between 0°C and +5°C, and advantageously in the presence of tertiary amine, like e.g. a Hünig-base.

Alternatively, the 3,4-diester-1-methylpyrrole of Scheme 6 may be obtained according to R.K.Huisgen, US 3,285,931) as outlined in scheme 7.

Scheme 7



Surprisingly, it has now been found that the novel compounds of formula I have, for practical purposes, a very advantageous spectrum of activities for protecting plants against diseases that are caused by fungi as well as by bacteria and viruses.

The compounds of formula I can be used in the agricultural sector and related fields of use as active ingredients for controlling plant pests. The novel compounds are distinguished by excellent activity at low rates of application, by being well tolerated by plants and by being environmentally safe. They have very useful curative, preventive and systemic properties and are used for protecting numerous cultivated plants. The compounds of formula I can be used to inhibit or destroy the pests that occur on plants or parts of plants (fruit, blossoms, leaves, stems, tubers, roots) of different crops of useful plants, while at the same time protecting also those parts of the plants that grow later e.g. from phytopathogenic micro-organisms.

It is also possible to use compounds of formula I as dressing agents for the treatment of plant propagation material, in particular of seeds (fruit, tubers, grains) and plant cuttings (e.g. rice), for the protection against fungal infections as well as against phytopathogenic fungi occurring in the soil.

The compounds I are, for example, effective against the phytopathogenic fungi of the following classes: Fungi imperfecti (e.g. *Botrytis*, *Pyricularia*, *Helminthosporium*, *Fusarium*, *Septoria*, *Cercospora* and *Alternaria*) and Basidiomycetes (e.g. *Rhizoctonia*, *Hemileia*, *Puccinia*). Additionally, they are also effective against the Ascomycetes classes (e.g. *Venturia* and *Erysiphe*, *Podosphaera*, *Monilinia*, *Uncinula*) and of the Oomycetes classes (e.g. *Phytophthora*, *Pythium*, *Plasmopara*). Outstanding activity has been observed against powdery mildew (*Erysiphe* spp.). Furthermore, the novel compounds of formula I are effective against phytopathogenic bacteria and viruses (e.g. against *Xanthomonas* spp, *Pseudomonas* spp, *Erwinia amylovora* as well as against the tobacco mosaic virus).

Within the scope of present invention, target crops to be protected typically comprise the following species of plants: cereal (wheat, barley, rye, oat, rice, maize, sorghum and related species); beet (sugar beet and fodder beet); pomes, drupes and soft fruit (apples, pears, plums, peaches, almonds, cherries, strawberries, raspberries and blackberries); leguminous plants (beans, lentils, peas, soybeans); oil plants (rape, mustard, poppy, olives, sunflowers, coconut, castor oil plants, cocoa beans, groundnuts); cucumber plants (pumpkins, cucumbers, melons); fibre plants (cotton, flax, hemp, jute); citrus fruit (oranges, lemons, grapefruit, mandarins); vegetables (spinach, lettuce, asparagus, cabbages, carrots, onions, tomatoes, potatoes, paprika); lauraceae (avocado, cinnamomum, camphor) or plants such as tobacco, nuts, coffee, eggplants, sugar cane, tea, pepper, vines, hops, bananas and natural rubber plants, as well as ornamentals.

The compounds of formula I are used in unmodified form or, preferably, together with the adjuvants conventionally employed in the art of formulation. To this end they are conveniently formulated in known manner to emulsifiable concentrates, coatable pastes, directly sprayable or dilutable solutions, dilute emulsions, wettable powders, soluble powders, dusts, granulates, and also encapsulations e.g. in polymeric substances. As with the type of the compositions, the methods of application, such as spraying, atomising, dusting, scattering, coating or pouring, are chosen in accordance with the intended objectives and the prevailing circumstances. The compositions may also contain further adjuvants such as stabilizers, antifoams, viscosity regulators, binders or tackifiers as well as fertilizers, micronutrient donors or other formulations for obtaining special effects.

Suitable carriers and adjuvants can be solid or liquid and are substances useful in formulation technology, e.g. natural or regenerated mineral substances, solvents, dispersants, wetting agents, tackifiers, thickeners, binders or fertilizers. Such carriers are for example described in WO 97/33890.

The compounds of formula I are normally used in the form of compositions and can be applied to the crop area or plant to be treated, simultaneously or in succession with further compounds. These further compounds can be e.g. fertilizers or micronutrient donors or other preparations which influence the growth of plants. They can also be selective herbicides as well as insecticides, fungicides, bactericides, nematocides, molluscicides or mixtures

of several of these preparations, if desired together with further carriers, surfactants or application promoting adjuvants customarily employed in the art of formulation.

The compounds of formula I can be mixed with other fungicides, resulting in some cases in unexpected synergistic activities. Mixing components which are particularly preferred are azoles, such as azaconazole, BAY 14120, bitertanol, bromuconazole, cyproconazole, difenoconazole, diniconazole, epoxiconazole, fenbuconazole, fluquinconazole, flusilazole, flutriafol, hexaconazole, imazalil, imibenconazole, ipconazole, metconazole, myclobutanil, pefurazoate, penconazole, pyrifenoxy, prochloraz, propiconazole, simeconazole, tebuconazole, tetraconazole, triadimefon, triadimenol, triflumizole, triticonazole; pyrimidinyl carbinole, such as ancymidol, fenarimol, nuarimol; 2-amino-pyrimidines, such as bupirimate, dimethirimol, ethirimol; morpholines, such as dodemorph, fenpropidine, fenpropimorph, spiroxamine, tridemorph; anilinopyrimidines, such as cyprodinil, mepanipyrim, pyrimethanil; pyrroles, such as fenpiclonil, fludioxonil; phenylamides, such as benalaxyl, furalaxyl, metalaxyl, R-metalaxyl, ofurace, oxadixyl; benzimidazoles, such as benomyl, carbendazim, debacarb, fuberidazole, thiabendazole; dicarboximides, such as chlozolate, dichlozoline, iprodione, myclozoline, procymidone, vinclozoline; carboxamides, such as carboxin, fenfuram, flutolanil, mepronil, oxycarboxin, thifluzamide; guanidines, such as guazatine, dodine, iminoctadine; strobilurines, such as azoxystrobin, kresoxim-methyl, metominostrobin, SSF-129, trifloxystrobin, picoxystrobin, BAS 500F (proposed name pyraclostrobin), BAS 520; dithiocarbamates, such as ferbam, mancozeb, maneb, metiram, propineb, thiram, zineb, ziram; N-halomethylthiotetrahydrophthalimides, such as captafol, captan, dichlofluanid, fluoromides, folpet, tolyfluanid; Cu-compounds, such as Bordeaux mixture, copper hydroxide, copper oxychloride, copper sulfate, cuprous oxide, mancozeb, oxine-copper; nitrophenol-derivatives, such as dinocap, nitrothal-isopropyl; organo-p-derivatives, such as edifenphos, iprobenphos, isoprothiolane, phosdiphen, pyrazophos, tolclofomethyl; various others, such as acibenzolar-S-methyl, anilazine, benthiallathion, blastocidin-S, chinomethionate, chloroneb, chlorothalonil, cyflufenamid, cymoxanil, dichlorone, diclomezine, dicloran, diethofencarb, dimethomorph, SYP-LI90 (proposed name: flumorph), dithianon, ethaboxam, etridiazole, famoxadone, fenamidone, fenoxanil, fentin, ferimzone, fluazinam, flusulfamide, fenhexamid, fosetyl-aluminium, hymexazol, iprovalicarb, IKF-916 (cyazofamid), kasugamycin, methasulfocarb, metrafenone, nicobifen, pencycuron, phthalide, polyoxins, probenazole, propamocarb, pyroquilon, quinoxifen, quintozone, sulfur, triazoxide, tricyclazole, triforine, validamycin, zoxamide (RH7281).

A preferred method of applying a compound of formula I, or an agrochemical composition which contains at least one of said compounds, is foliar application. The frequency of application and the rate of application will depend on the risk of infestation by the corresponding pathogen. However, the compounds of formula I can also penetrate the plant through the roots via the soil (systemic action) by drenching the locus of the plant with a liquid formulation, or by applying the compounds in solid form to the soil, e.g. in granular form (soil application). In crops of water rice such granulates can be applied to the flooded rice field. The compounds of formula I may also be applied to seeds (coating) by impregnating the seeds or tubers either with a liquid formulation of the fungicide or coating them with a solid formulation.

The formulation, i.e. the compositions containing the compound of formula I and, if desired, a solid or liquid adjuvant, are prepared in known manner, typically by intimately mixing and/or grinding the compound with extenders, e.g. solvents, solid carriers and, optionally, surface active compounds (surfactants).

The agrochemical formulations will usually contain from 0.1 to 99 % by weight, preferably from 0.1 to 95 % by weight, of the compound of formula I, 99.9 to 1 % by weight, preferably 99.8 to 5 % by weight, of a solid or liquid adjuvant, and from 0 to 25 % by weight, preferably from 0.1 to 25 % by weight, of a surfactant.

Advantageous rates of application are normally from 5 g to 2 kg of active ingredient (a.i.) per hectare (ha), preferably from 10 g to 1 kg a.i./ha, most preferably from 20 g to 600 g a.i./ha. When used as seed drenching agent, convenient dosages are from 10 mg to 1 g of active substance per kg of seeds.

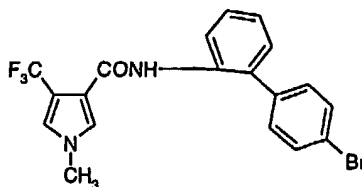
Whereas it is preferred to formulate commercial products as concentrates, the end user will normally use dilute formulations.

The following non-limiting Examples illustrate the above-described invention in more detail. Temperatures are given in degrees Celsius. The following abbreviations are used:  
m.p.= melting point; b.p.= boiling point. "NMR" means nuclear magnetic resonance

spectrum. MS stands for mass spectrum. "%" is percent by weight, unless corresponding concentrations are indicated in other units.

### Example 1

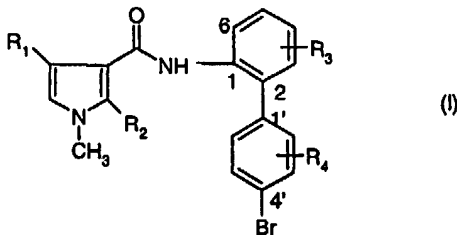
#### 1-Methyl-4-trifluoromethyl-1H-pyrrole-3-carboxylic acid (4'-bromobiphenyl-2-yl) amide



A solution of 1-methyl-4-trifluoromethyl-1H-pyrrole-3-carboxylic acid (0.42 g, 2.2 mmol) and oxalyl chloride (0.30 g, 2.4 mmol) in methylene chloride (20 ml) is stirred for 3 hours at room temperature in the presence of a catalytic amount of DMF. Then the resulting acid chloride solution is slowly added to a solution of 2-(4'-bromophenyl)aniline (0.55 g, 2.2 mmol) and triethylamine (0.33 g, 3.3 mmol) in 15 ml of methylene chloride. The resulting mixture is then stirred for 16 hours at room temperature. After the addition of ethylacetate, the organic phase is washed twice with water. After drying the organic phase over  $\text{Na}_2\text{SO}_4$ , the solvent is removed in a water-jet-vacuum and the obtained crude product is finally purified by column chromatography (silica gel; eluant: ethylacetate/hexane=1:2). 0.52 g of 1-methyl-4-trifluoromethyl-1H-pyrrole-3-carboxylic acid (4'-bromobiphenyl-2-yl) amide are obtained in the form of a yellow powder having a melting point of 163-164°C.

The following compounds of formula I are prepared in a similar way, using analogous methods.

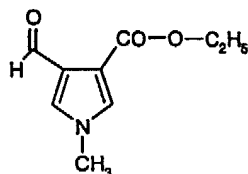
Table 1



Compd. No.	R <sub>1</sub>	R <sub>2</sub>	R <sub>3</sub>	R <sub>4</sub>	phys.data, m.p. °C
1.1	CF <sub>3</sub>	H	H	H	163-164
1.2	CF <sub>2</sub> H	H	H	H	166-167

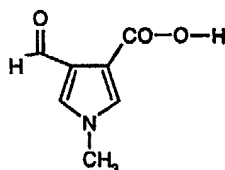
1.3	CFH <sub>2</sub>	H	H	H	
1.4	CF <sub>3</sub>	F	H	H	resin, M <sup>+</sup> =411
1.5	CF <sub>2</sub> H	F	H	H	resin, M <sup>+</sup> =423
1.6	CFH <sub>2</sub>	F	H	H	
1.7	CF <sub>3</sub>	H	6-F	H	
1.8	CF <sub>2</sub> H	H	6-F	H	
1.9	CF <sub>3</sub>	F	6-F	H	
1.10	CF <sub>2</sub> H	F	6-F	H	

**Example 2:** 4-Formyl-1-methyl-1H-pyrrole-carboxylic acid ethylester



A solution of 21.6 g (0.11 mol) 1-methyl-1H-pyrazole-3,4-dicarboxylic acid monoethylester and 14.9 g (0.117 mol) oxalyl chloride and 150 ml methylene chloride is stirred for 3 hours at room temperature in the presence of a catalytic amount of absolute DMF. After 3 hours the solvent is removed in a water jet vacuum and the crude acid chloride (21.5 g) is dissolved in 400 ml of dry tetrahydrofuran. After addition of 14.2 g (0.11 mol) of N,N-diisopropylethylamine (Hünig-base) the mixture is hydrogenated with hydrogen in the presence of 6.0 g 10% Pd/C at 0°-5°C for 5 ½ hours. Then the catalyst is filtered off and the solvent removed in a water jet vacuum. The raw material is purified by flash-chromatography over silica gel (eluant: t-butylmethylether/hexane 1:5). Yield: 16 g 4-formyl-1-methyl-1H-pyrrole carboxylic acid ethylester in the form of a yellow powder; m.p.: 75°-76°C.

**Example 3:** 4-Formyl-1-methyl-1H-pyrrole-carboxylic acid

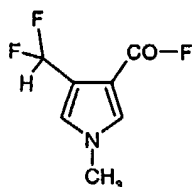


To a solution of 4.6 g (0.0255 mol) 4-formyl-1-methyl-1H-pyrrole-carboxylic acid ethylester and 90 ml of ethanol is added a solution of 2.1 g (0.031 mol) potassium hydroxide of 85% and 20 ml of water producing a slightly exothermic reaction. The resulting mixture is stirred

for 2 hours at +80°C and then the solvent mixture EtOH/H<sub>2</sub>O is distilled off in vacuo. The resulting oil is dissolved in 100 ml of H<sub>2</sub>O and washed twice with ethylacetate. Then 20 ml of 2N hydrogen chloride solution is added slowly of the water phase in the cold. The precipitated solid is filtered off and washed with water. After drying of the precipitate in a vacuum oven the pure acid is obtained. Yield: 3.6 g of 4-formyl-1-methyl-1H-pyrrole-carboxylic acid in the form of a slightly yellow powder; m.p.: 178°-180°C.

### Example 3

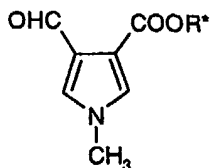
#### 4-Difluoromethyl-1-methyl-1H-pyrrole-3-carbonyl fluoride



To a cooled solution of 2.6 g (0.017 mol) 4-formyl-1-methyl-1H-pyrrole-carboxylic acid and 70 ml methylene chloride is added a solution of 11.0 g (0.068 mol) diethylaminosulfurtrifluoride (DAST) and 10 ml methylenechloride in such a manner that the temperature remains constant at 0° to +2°C. Then the mixture is stirred for 30 minutes at 0°C and 16 hours at room temperature. The reaction mixture is taken up in ethylacetate and washed twice with ice water and brine. After drying the solvent is removed in a water jet vacuum and the residue purified by flash chromatography over silica gel (eluant: hexane/ethylacetate, 2:1). Yield: 1.95 g 4-difluoromethyl-1-methyl-1H-pyrrole-3-carbonyl fluoride in the form of a brownish solid; m.p.: 53°-54°C.

In a similar manner the intermediates of the general formula B of table 2 may be obtained.

Table 2



Compound. No.	R*	phys. Data (m.p. [°C] )
1.1	CH <sub>3</sub>	
1.2	C <sub>2</sub> H <sub>5</sub>	76-77

1.3	$C_3H_7-n$	
1.4	$C_4H_9-n$	
1.5	$C_6H_{13}-n$	
1.6	$Si(CH_3)_3$	

Formulation Examples for compounds of formula I

Working procedures for preparing formulations of the compounds of formula I such as Emulsifiable concentrates, Solutions, Granulates, Dusts and Wettable powders are described in WO 97/33890.

Biological Examples: Fungicidal actions

Example B-1: Action against *Puccinia recondita* / wheat (Brownrust on wheat)

1 week old wheat plants cv. Arina are treated with the formulated test compound (0.02% active ingredient) in a spray chamber. One day after application wheat plants are inoculated by spraying a spore suspension ( $1 \times 10^5$  uredospores/ml) on the test plants. After an incubation period of 2 days at 20° C and 95% r. h. plants are kept in a greenhouse for 8 days at 20° C and 60% r.h. The disease incidence is assessed 10 days after inoculation.

Compounds of Table 1 show good activity in this test (< 20% infestation). Infestation is prevented virtually completely (0-5% infestation) with compounds 1.1, 1.2, 1.4 and 1.5.

Example B-2: Action against *Podosphaera leucotricha* / apple (Powdery mildew on apple)

5 week old apple seedlings cv. McIntosh are treated with the formulated test compound (0.002% active ingredient) in a spray chamber. One day after application apple plants are inoculated by shaking plants infected with apple powdery mildew above the test plants. After an incubation period of 12 days at 22° C and 60% r. h. under a light regime of 14/10 h (light/dark) the disease incidence is assessed.

Compounds of Table 1 show good activity in this test . The compounds 1.1, 1.2, 1.4 and 1.5 exhibit strong efficacy (< 20% infestation).

Example B-3: Action against *Venturia inaequalis* / apple (Scab on apple)

4 week old apple seedlings cv. McIntosh are treated with the formulated test compound (0.02% active ingredient) in a spray chamber. One day after application apple plants are inoculated by spraying a spore suspension ( $4 \times 10^5$  conidia/ml) on the test plants. After an incubation period of 4 days at 21° C and 95% r. h. the plants are placed for 4 days at 21° C and 60% r. h. in a greenhouse. After another 4 day incubation period at 21° C and 95% r. h. the disease incidence is assessed.

Compounds of Table 1 show good activity in this test . The compounds 1.1, 1.2, 1.4 and 1.5 exhibit strong efficacy (< 20% infestation).

Example B-4: Action against *Erysiphe graminis* / barley (Powdery mildew on barley)

1 week old barley plants cv. Express are treated with the formulated test compound (0.02% active ingredient) in a spray chamber. One day after application barley plants are inoculated by shaking powdery mildew infected plants above the test plants. After an incubation period of 6 days at 20°C / 18°C (day/night) and 60% r. h. in a greenhouse the disease incidence is assessed.

Compounds of Table 1 show good activity in this test . The compounds 1.1, 1.2, 1.4 and 1.5 exhibit strong efficacy (< 20% infestation).

Example B-5: Action against *Botrytis cinerea* / apple (Botrytis on apple fruits)

In an apple fruit cv. Golden Delicious 3 holes are drilled and each filled with 30 µl droplets of the formulated test compound (0.002% active ingredient). Two hours after application 50 µl of a spore suspension of *B. cinerea* ( $4 \times 10^5$  conidia/ml) are pipetted on the application sites. After an incubation period of 7 days at 22° C in a growth chamber the disease incidence is assessed.

Compounds of Table 1 show good activity in this test . The compounds 1.1, 1.2, 1.4 and 1.5 exhibit very strong efficacy (< 10% infestation).

Example B-6: Action against *Botrytis cinerea* / grape (Botrytis on grapes)

5 week old grape seedlings cv. Gutedel are treated with the formulated test compound (0.002% active ingredient) in a spray chamber. Two days after application grape plants are inoculated by spraying a spore suspension ( $1 \times 10^8$  conidia/ml) on the test plants. After an

incubation period of 4 days at 21° C and 95% r. h. in a greenhouse the disease incidence is assessed.

Compounds of Table 1 show good activity in this test . The compounds 1.1, 1.2, 1.4 and 1.5 exhibit very strong efficacy (< 10% infestation).

Example B-7: Action against *Botrytis cinerea* / tomato (Botrytis on tomatoes)

4 week old tomato plants cv. Roter Gnom are treated with the formulated test compound (0.002% active ingredient) in a spray chamber. Two days after application tomato plants are inoculated by spraying a spore suspension ( $1 \times 10^5$  conidia/ml) on the test plants. After an incubation period of 4 days at 20° C and 95% r. h. in a growth chamber the disease incidence is assessed.

Compounds of Table 1 show good activity in this test . The compounds 1.1, 1.2, 1.4 and 1.5 exhibit very strong efficacy (< 10% infestation).

Example B-8: Action against *Pyrenophora teres* / barley (Net blotch on barley)

1 week old barley plants cv. Express are treated with the formulated test compound (0.002% active ingredient) in a spray chamber. Two days after application barley plants are inoculated by spraying a spore suspension ( $3 \times 10^4$  conidia/ml) on the test plants. After an incubation period of 2 days at 20° C and 95% r. h. plants are kept for 2 days at 20° C and 60% r.h. in a greenhouse. The disease incidence is assessed 4 days after inoculation.

Compounds of Table 1 show good activity in this test . The compounds 1.1, 1.2, 1.4 and 1.5 exhibit strong efficacy (< 20% infestation).

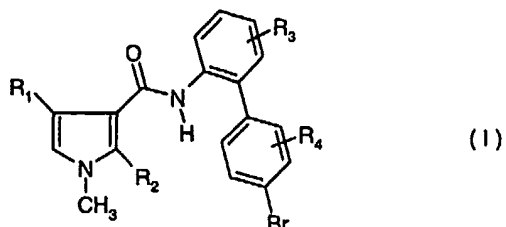
Example B-9: Action against *Septoria nodorum* / wheat (Septoria leaf spot on wheat)

1 week old wheat plants cv. Arina are treated with the formulated test compound (0.02% active ingredient) in a spray chamber. One day after application wheat plants are inoculated by spraying a spore suspension ( $5 \times 10^5$  conidia/ml) on the test plants. After an incubation period of 1 day at 20° C and 95% r. h. plants are kept for 10 days at 20° C and 60% r.h. in a greenhouse. The disease incidence is assessed 11 days after inoculation.

Compounds of Table 1 show good activity in this test . The compounds 1.1, 1.2, 1.4 and 1.5 exhibit strong efficacy (< 20% infestation).

What is claimed is

1. A pyrrolecarboxamide of formula I



wherein

R<sub>1</sub> is CF<sub>3</sub>, CF<sub>2</sub>H or CFH<sub>2</sub>;

R<sub>2</sub> is hydrogen or fluoro;

R<sub>3</sub> is hydrogen or fluoro; and

R<sub>4</sub> is hydrogen, fluoro, chloro, bromo, methyl, CF<sub>3</sub>, OCF<sub>3</sub> or SCF<sub>3</sub>.

2. A compound of formula I according to claim 1, wherein

R<sub>4</sub> is hydrogen, chloro, methyl, CF<sub>3</sub> or OCF<sub>3</sub>.

3. A compound of formula I according to claim 2, wherein

R<sub>2</sub> is hydrogen.

4. A compound of formula I according to claim 2, wherein

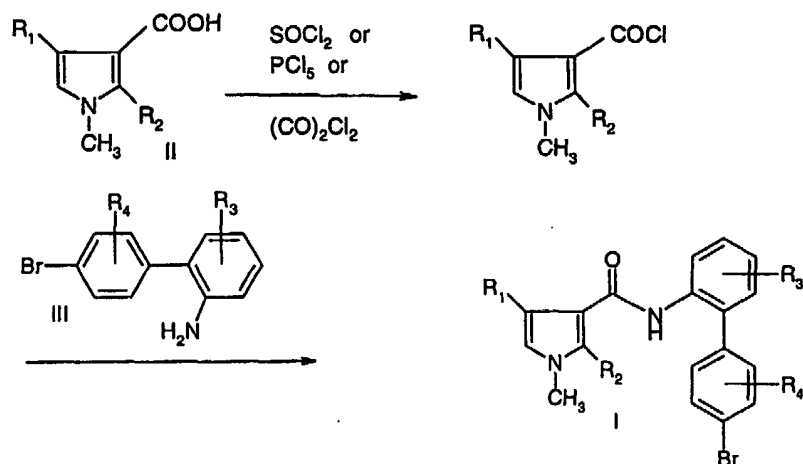
R<sub>2</sub> is fluoro.

5. A compound of formula I according to claim 1 selected from the group comprising

1-methyl-4-trifluoromethyl-1H-pyrrole-3-carboxylic acid (4'bromobiphenyl-2-yl) amide or

1-methyl-4-difluoromethyl-1H-pyrrole-3-carboxylic acid (4'bromobiphenyl-2-yl) amide.

6. A process for the preparation of compounds of formula I which comprises reacting the starting materials according to the scheme

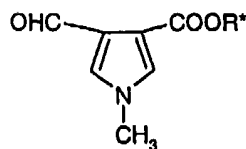


wherein  $R_1$ ,  $R_2$ ,  $R_3$  and  $R_4$  are as defined for formula I in claim 1.

7. A composition for controlling microorganisms and preventing attack and infestation of plants therewith, wherein the active ingredient is a compound as claimed in claim 1 together with a suitable carrier.

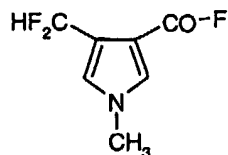
8. A method of controlling or preventing infestation of cultivated plants by phytopathogenic microorganisms by application of a compound of formula I as claimed in claim 1 to plants, to parts thereof or the locus thereof.

9. A compound of the general formula

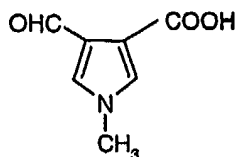


wherein  $R^*$  is hydrogen,  $\text{C}_1$ - $\text{C}_6$ alkyl, or  $\text{Si}(\text{C}_1\text{-C}_6\text{alkyl})_3$ .

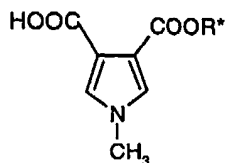
10. The compound of the formula



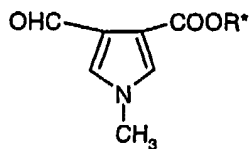
11. A process for the preparation of a compound of the formula



which process comprises reducing a compound of the formula



wherein R\* is C<sub>1</sub>-C<sub>6</sub>alkyl, or Si(C<sub>1</sub>-C<sub>6</sub>alkyl)<sub>3</sub>, in a two-step process by reacting it first with a halogenating agent selected from SOCl<sub>2</sub>/ dimethylformamide and oxalic acid chloride/ dimethylformamide, and in a second step reducing the intermediate acid chloride with palladium on carbon in the presence of a base, and hydrolyzing the resulting ester of the formula



wherein R\* is C<sub>1</sub>-C<sub>6</sub>alkyl, or Si(C<sub>1</sub>-C<sub>6</sub>alkyl)<sub>3</sub> under alkaline conditions.

# INTERNATIONAL SEARCH REPORT

International Application No  
PCT/EP 02/01344

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07D207/34 A01N43/36

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07D A01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, BEILSTEIN Data, CHEM ABS Data

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 00 09482 A (NOVARTIS ERFINDE VERWALT GMBH ; EBERLE MARTIN (CH); NOVARTIS AG (CH)) 24 February 2000 (2000-02-24) cited in the application example P1 table 1 examples 1.02, 1.03; table 12 claim 7; examples 2, 3 claims 1, 10-12 ---	1-5, 7, 8
Y	WO 97 08148 A (BASF AG ; EICKEN KARL (DE); RANG HARALD (DE); HARREUS ALBRECHT (DE)) 6 March 1997 (1997-03-06) example 1.182; table 1 examples 3.9, 3.10, 3.19, 3.20; table 3 claims 3-6 --- -/-	1-5, 7, 8

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

### \* Special categories of cited documents:

- 'A' document defining the general state of the art which is not considered to be of particular relevance
- 'E' earlier document but published on or after the international filing date
- 'L' document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- 'O' document referring to an oral disclosure, use, exhibition or other means
- 'P' document published prior to the international filing date but later than the priority date claimed

- 'T' later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- 'X' document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- 'Y' document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- '&' document member of the same patent family

Date of the actual completion of the international search

10 June 2002

Date of mailing of the international search report

21/06/2002

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax. (+31-70) 340-3016

Authorized officer

Seitner, I

# INTERNATIONAL SEARCH REPORT

International Application No  
PCT/EP 02/01344

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	EP 0 219 756 A (CELAMERCK GMBH & CO KG) 29 April 1987 (1987-04-29) example 2; table C claims 7-9	1-5,7,8

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/EP 02/01344

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 0009482	A	24-02-2000	AU 5513899 A BR 9912962 A CN 1311774 T WO 0009482 A1 EP 1105375 A1 PL 345823 A1 TR 200100478 T2 US 2002019541 A1	06-03-2000 08-05-2001 05-09-2001 24-02-2000 13-06-2001 14-01-2002 21-06-2001 14-02-2002
WO 9708148	A	06-03-1997	DE 19531813 A1 AU 6928596 A WO 9708148 A1 EP 0847388 A1 JP 11511449 T US 5998450 A	06-03-1997 19-03-1997 06-03-1997 17-06-1998 05-10-1999 07-12-1999
EP 0219756	A	29-04-1987	DE 3536029 A1 DE 3541718 A1 DE 3615447 A1 AT 99682 T AU 6360886 A AU 654470 B2 AU 6599990 A BR 8604917 A CA 1290326 A1 CZ 8607259 A3 DD 258170 A5 DE 3689506 D1 DK 480286 A EP 0219756 A1 ES 2061432 T3 FI 864062 A HU 43997 A2 IE 63475 B IL 80257 A JP 2048027 C JP 7072164 B JP 62103051 A KR 9409529 B1 NZ 217845 A PT 83504 A ,B US 4910200 A YU 172586 A1 ZA 8607662 A	09-04-1987 27-05-1987 12-11-1987 15-01-1994 16-04-1987 10-11-1994 11-04-1991 07-07-1987 08-10-1991 11-09-1996 13-07-1988 17-02-1994 10-04-1987 29-04-1987 16-12-1994 10-04-1987 28-01-1988 19-04-1995 21-11-1991 25-04-1996 02-08-1995 13-05-1987 14-10-1994 26-07-1990 01-11-1986 20-03-1990 31-10-1988 29-06-1988